<u>REMARKS</u>

On March 12, 2008, Applicants' representatives, Drs. Kristina Bieker-Brady and Todd Armstrong, participated in a telephonic interview with Examiner Sisson during which a draft supplemental response that included proposed amendments to pending claims 27, 30-33, 44, and 47-49 was discussed. The Interview Summary, dated March 27, 2008 (the "Interview Summary"), provides the Office's summary of the substance of the interview. In response to the Interview Summary, Applicants wish to supplement the record with the following remarks.

On the continuation sheet (PTOL-413) appended to the Interview Summary, the Office states that "Mr. Sisson noted that Brennan does disclose probes that would perform in the claimed assay. Dr. Beiker-Brady [sic] indicated that the method probably would not be diagnostic if one only used 10-mers." The point being made by Dr. Bieker-Brady during the telephonic interview was not that 10-mers would not be diagnostic if used in the method of present independent claims 27 and 48, but rather that the array of Brennan (U.S. Patent No. 5,474,796), which includes only 10-mers and all possible 10-mers, would not allow one to determine the presence or absence of a given, predefined pathological condition in a subject being tested. Because the Brennan array includes *every* permutation of 10-mer nucleic acid sequences, it would bind *every species* of nucleic acid molecule present in a sample containing a diverse population of nucleic acid molecules, e.g., a population of cDNA molecules prepared from nucleic acid molecules (e.g., RNAs) from nucleated blood cells of a subject, even those nucleic acid molecules not indicative of a given, predefined pathological condition.[1] Thus, the Brennan array would be incapable of detecting whether a sample containing a diverse population of nucleic acid molecules contains differentially spliced ribonucleic acid molecules (RNAs) indicative of a given, predefined pathological condition, as is required by the method of present independent claims 27 and 48, and claims dependent therefrom, regardless of the stringency conditions used during hybridization.

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1 In fact, Brennan clearly discloses that only a single species of "target nucleic acid" is to be applied to the Brennan array and not a diverse population of nucleic acid molecules because the purpose is to sequence the target nucleic acid molecule (see Example 4 of Brennan).

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The Interview Summary also suggests that Applicants' specification describes 10-mers for use in the methods of present independent claims 27 and 48, and claims dependent therefrom ("Mr. Sisson noted that page 13 of the originally-filed specification teaches using a complementary nucleic acid that is '10 nucleotides long so as to unambiguously identify the corresponding cDNA'"; see continuation sheet (PTOL-413)). Because Brennan fails to teach or suggest the method of independent claims 27 and 48, and claims dependent therefrom, as was acknowledged by the Office in the Interview Summary, Applicants believe it is irrelevant whether Applicants' specification does or does not disclose the use of 10-mers in the method of present independent claims 27 and 48. Applicants wish to clarify that page 13, lines 1-7, of the present specification discloses the use of serial analysis of gene expression (SAGE) as a method for identifying transcripts that are differentially expressed in a population of cells. As is explained below, the nucleic acid "label" having a length of about 10 bp in length is described by the present specification as being identified using SAGE.

SAGE involves isolating the RNA expressed by a population of cells, converting the RNA into cDNA, and cleaving the cDNA with a restriction enzyme to generate short sequence labels (also referred to as a "tags") of about 10-14 bp that contain sufficient information to uniquely identify its transcript, provided that that the label is obtained from a unique position within each transcript. The short sequence labels are then linked together to from long serial molecules that can be cloned and sequenced. It is the sequencing of the labels, and not their hybridization to other nucleic acid molecules, that allows one to determine the relative presence of a label among a population of label sequences, which directly correlates with the expression level of the transcript corresponding to the label. Thus, SAGE can be used to identify transcript sequences and to analyze their express levels in a population of cells. The use of SAGE for this purpose is clearly described in the present specification, which states that "[t]he labels are then assembled for sequencing and analysis [of expression levels] (Velculescu et al., Science, 1995, 270: 484-487). This approach therefore represents a short-cut to systematic sequencing" (page 13, lines 4-7, of the present specification). Thus, contrary to the Office's conclusion, page 13 of the present specification describe the use of a 10-mer nucleic acid sequence identified using SAGE to assess differential gene expression.
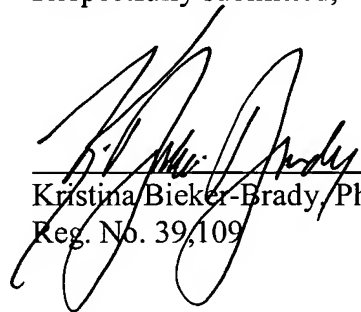
CONCLUSION

Applicants submit that the claims are now in condition for allowance, and such action is respectfully requested.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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